PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB 904 PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2005/002190	International filing date *(day/month/year)* 02.03.2005	Priority date *(day/month/year)* 25.03.2004
International Patent Classification (IPC) or both national classification and IPC INV. C07D459/00		
Applicant INDENA S.P.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.11.2005	10.04.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Baston, E Telephone No. +49 89 2399-8229

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP2005/002190

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-9 received on 07.11.2005 with letter of 07.11.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-10
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

To section V

The following documents were cited in the search report and were considered for the examination of the present application:

D1: GB 809 913 A (CIBA LIMITED) 4 March 1959,
D2: GB 868 478 A (LES LABORATOIRES FRANCAIS DE CHIMIOTHERAPIE) 17 May 1961,
D3: SAKAI, S.I. OGAWA, M.: "The Chemical Transformation to Deserpidine" HETEROCYCLES, vol. 10, 1978, pages 67-71,
D4: TAMIZ, A.P. ET AL.: "Structure-Activity Relationship for a ...Receptors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 9, 1999, pages 1619-1624.

The present application is directed to the preparation of Deserpidine, a natural product which is to be distinguished from Reserpine by the absence of a methoxy group in position 11. The process is characterized by the demethylation of a methoxy precursor (II) which results in the formation of a hydroxy intermediate (III), which is then reduced. Ring opening of the lactone and esterification results in the formation of the target molecule.

Document D4 deals with a demethylation process in general without mentioning intermediate (III). D1-D3 disclose preparation examples for Deserpidine. None of these documents uses a derivative bearing a methoxy group in position 11 which is then demethylated to a hydroxy intermediate according to formula (III). In view of this difference novelty is acknowledged for claims 1-7. Claims 8-9 are directed to intermediates with a hydroxy or a p-toluenesulfonate group in position 11, which are not anticipated by the prior art. Consequently claims 1-9 are novel (Art. 33(2) PCT).

None of the specified documents suggests the use of an intermediate (III) and thus the requirements of Art. 33(3) PCT are met.

Claim 1 was amended by incorporation of claim 2, thus clarifying that a precursor carrying a leaving group has to be present. The requirements of Art. 5 and 6 PCT are met.